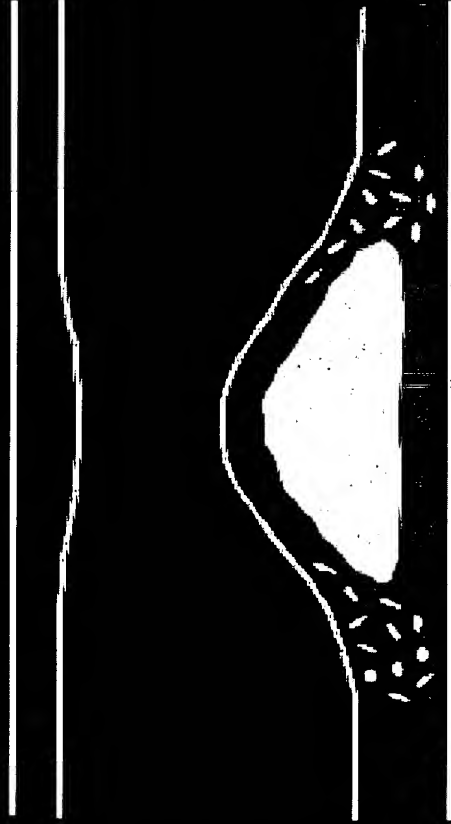# Vulnerable Plaque Characterization Using Temporal and Spatial Speckle Analysis

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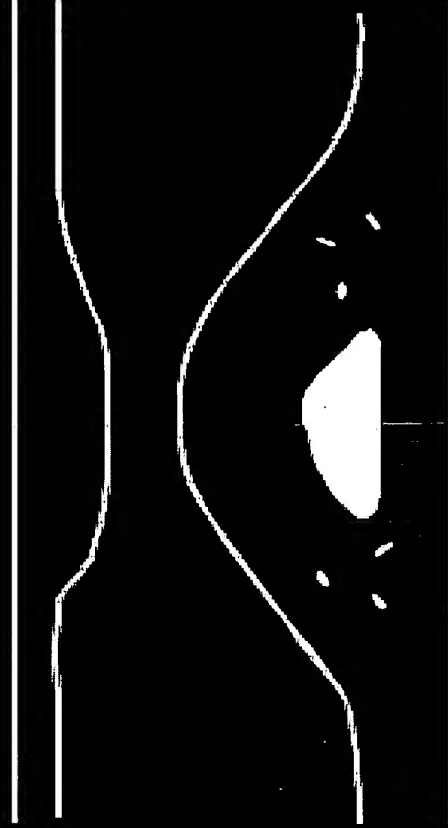Department of Pathology and

Wellman Laboratories of Photomedicine

Vulnerable Plaques

Vulnerable Plaque	Stable Plaque

Thin	Cap	Thick
Abundant	Macrophages	Few
High	Lipid Conc.	Low

Vulnerable Plaque Diagnosis

Proposed Diagnostics

- Infrared
  - Indirectly measures lipid content of plaque

- Fluorescence
  - Measures autofluorescence
    - Collagen
    - MMP

- IVUS
  - Structural measurement of cap
  - Poor resolution

- OCT
  - Structural measurement of cap
  - Sufficient resolution for measurement of cap thickness

Proposed methods do not measure the biomechanical properties of plaque

Intrinsic Plaque Biomechanics

Biomechanical properties

- Cap strength
  - Proportional to thickness and structural integrity

- Lipid pool
  - Shear stress and strain on cap are related to lipid pool stiffness
  - Rupture of plaque tends to occur in areas of large stiffness gradient between cap and lipid pool
  - Lipid lowering drugs increase stiffness of lipid pool
  - Stiffening of the lipid pool decreases vulnerability

Mechanical stiffness of the cap and lipid pool are essential parameters for assessing the likelihood of plaque rupture

Viscosity

Viscosity of tissue is proportional to stiffness

- Related to the ability of the molecules in the tissue matrix to move

Brownian motion

- Random motion of particles in the matrix
- Brownian motion is inversely proportional to viscosity and stiffness
  - Low stiffness, rapid Brownian motion
  - High stiffness, slow Brownian motion

Brownian motion velocity is a measurement of tissue stiffness

Speckle

Coherent interference of light remitted from a scattering media or substrate
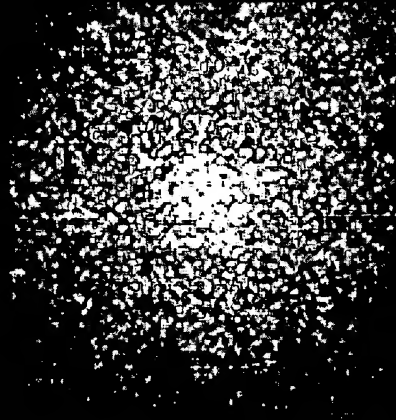
- Produces a grainy pattern at the surface of the specimen and in the image plane
- The pattern is created from the remitted field after many multiple scattering events within the specimen
- Motion of a single scatterer in the specimen changes the speckle pattern

Speckle Motion

**Motion of a single scatterer in the specimen changes the speckle pattern**

- The time dependent speckle pattern can be used to determine the Brownian motion within a multiply scattering media

- The motion is characterized by the spatial decorrelation of the speckle pattern as a function of time

- For Brownian motion, the decorrelation is a negative exponential with a time constant, τ

Stiffness of the cap and lipid pool can be determined by measuring the speckle decorrelation time constant

Light Diffusion

In tissue, light remitted further from the beam entry point has probed deeper into the tissue

- Governed by the optical properties of tissue
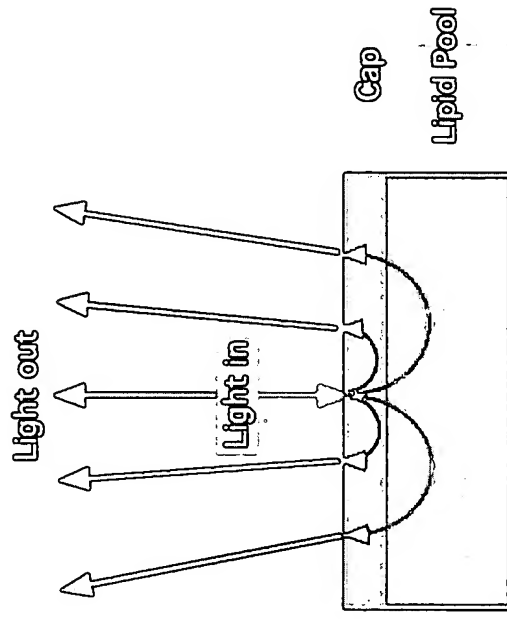
Spatial and Temporal Characterization of Plaques

Measuring the speckle decorrelation time, τ, as a function of distance from beam entry point allows measurement of Brownian Motion and
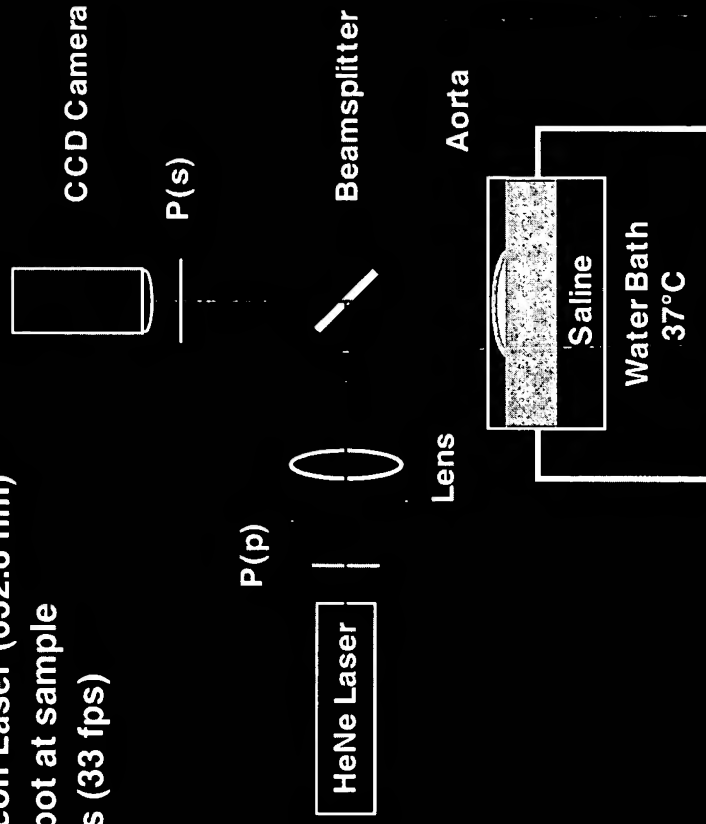
- Cap thickness
- Cap stiffness
- Lipid pool stiffness

Static

Modulated

Modulated

Modulated

Light in

Speckle Pattern

Cap

Lipid Pool
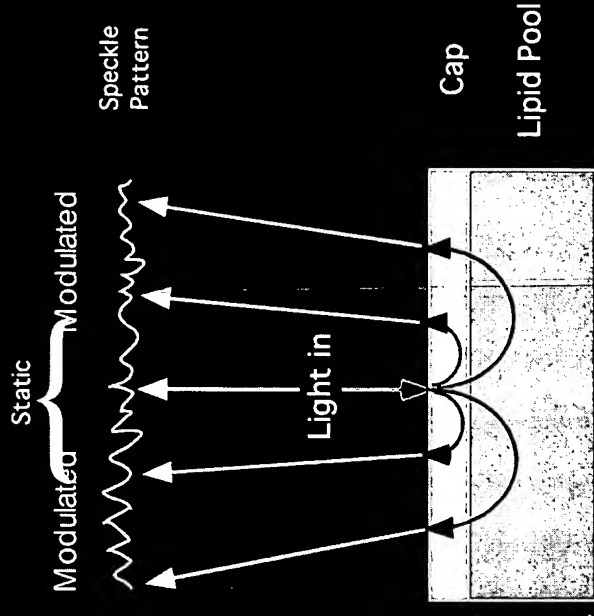
Proof of Principle

Methods

- Cadaveric aortas
- Normal saline, 37°C
- Helium Neon Laser (632.8 nm)
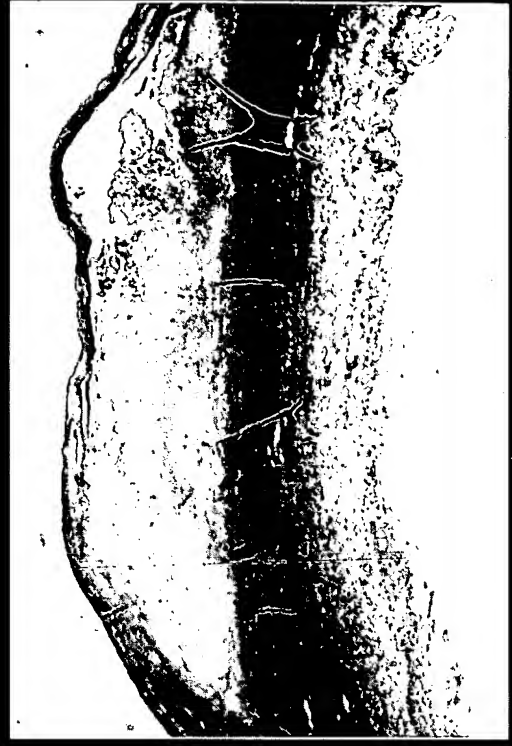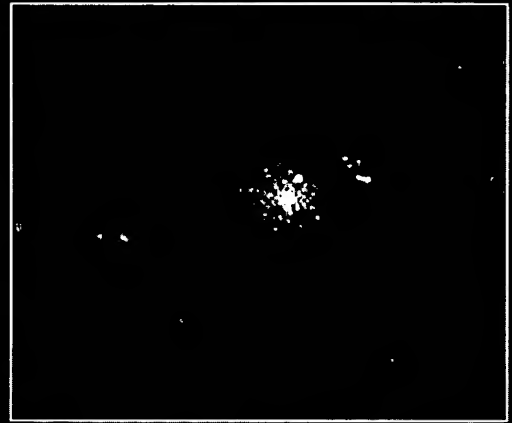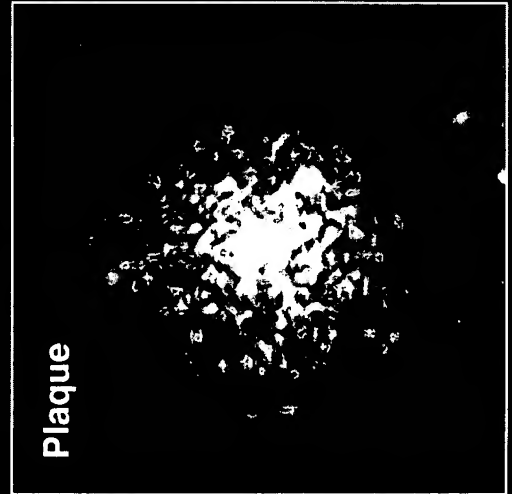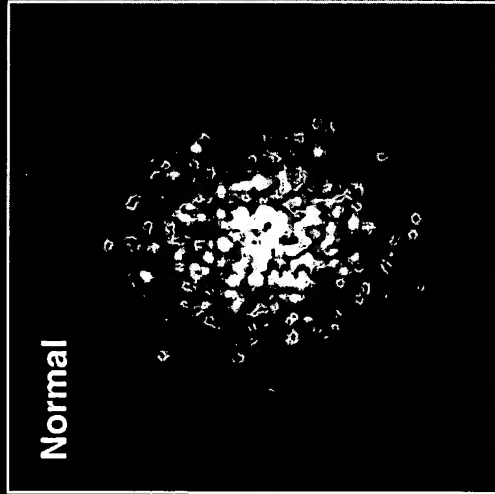- 100 μm spot at sample
- 2 seconds (33 fps)

Results

Speckle **Visible** **Histology**

Normal

Plaque

Results

Aortic Plaque vs. Normal Aorta
Speckle Correlation
(Perpendicular Polarization)
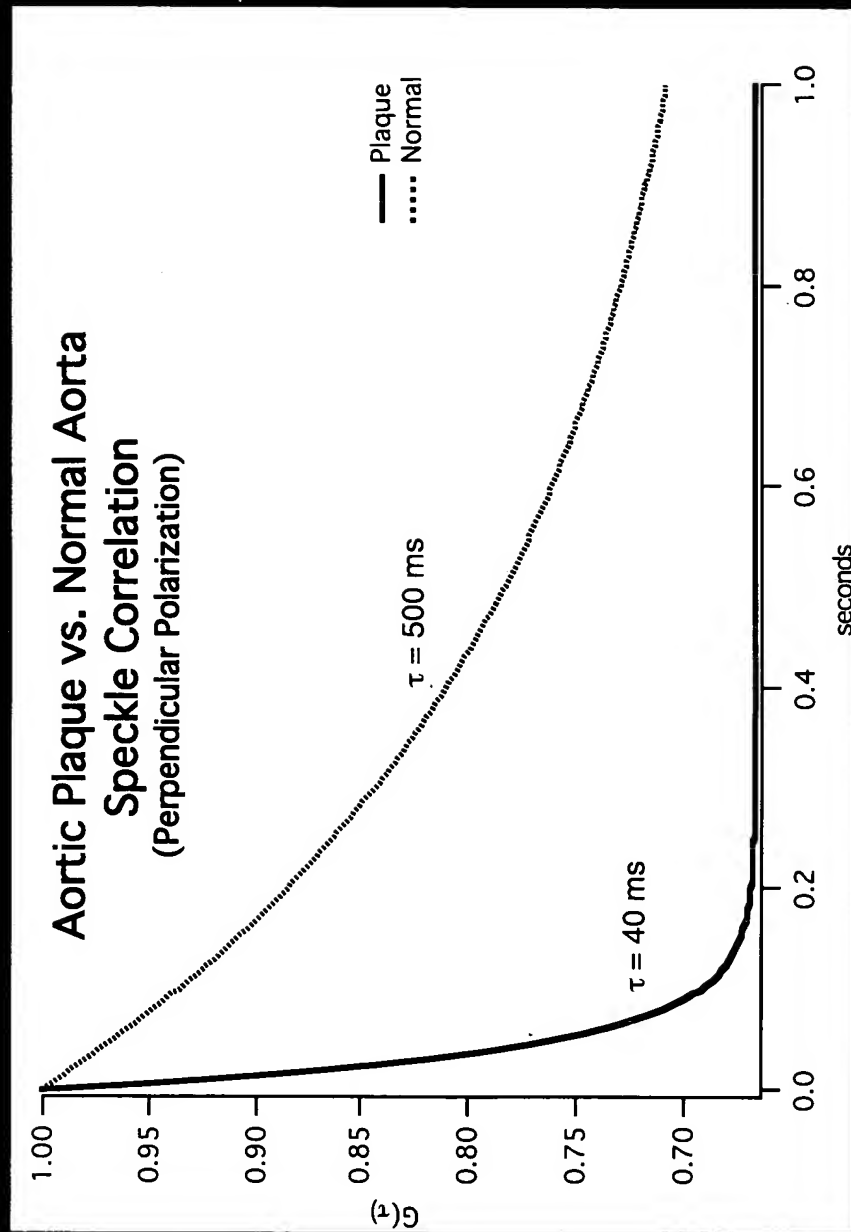
Results
(Aortic Plaques)

Speckle

Visible

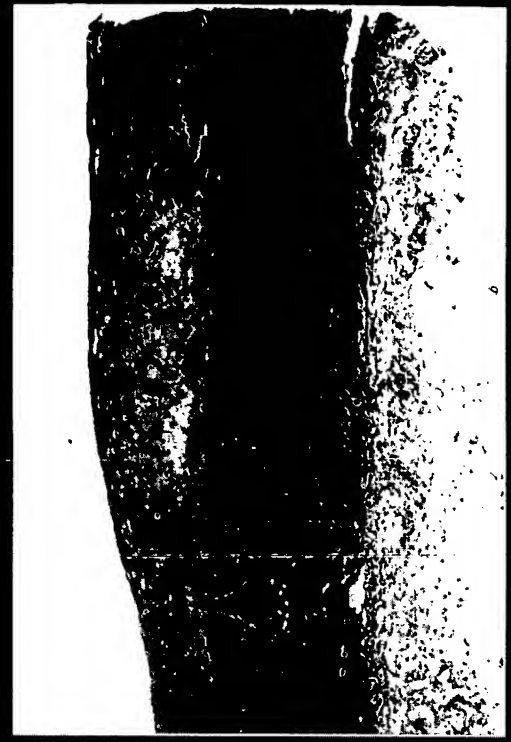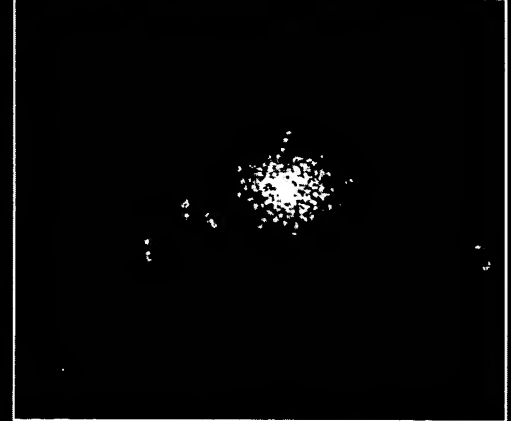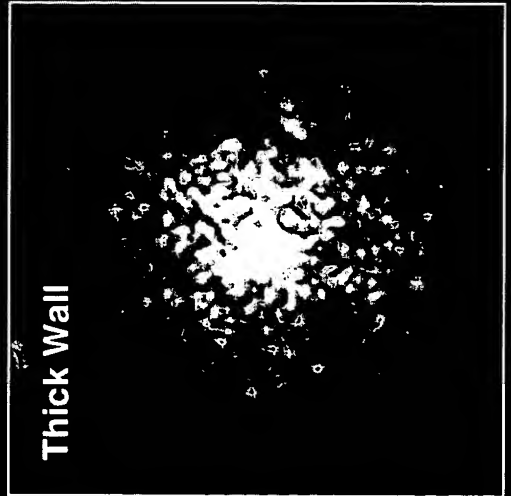**Histology**

Thin Wall
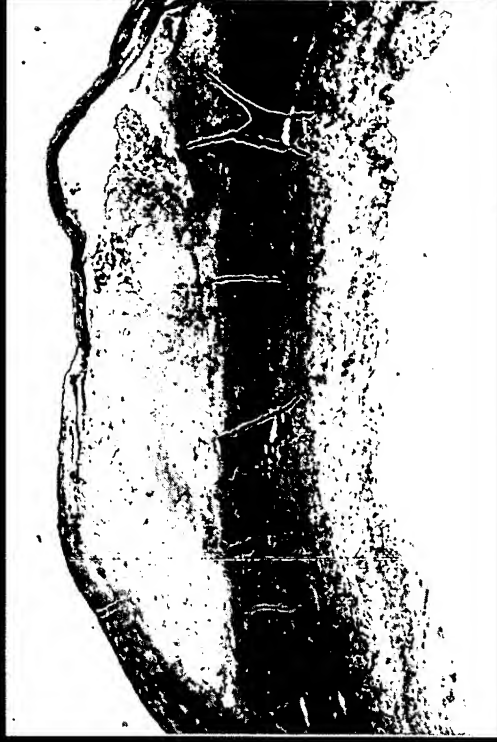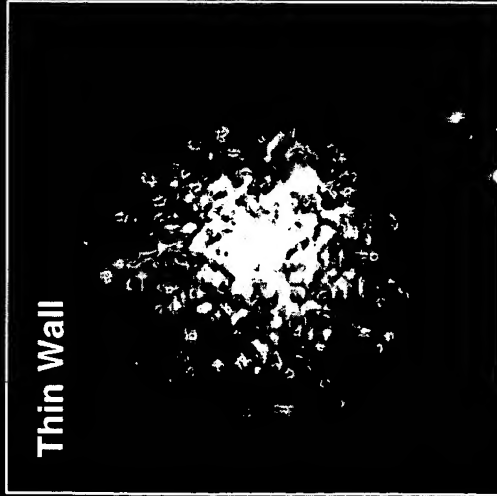
Thick Wall

Results
(Spatial Localization)
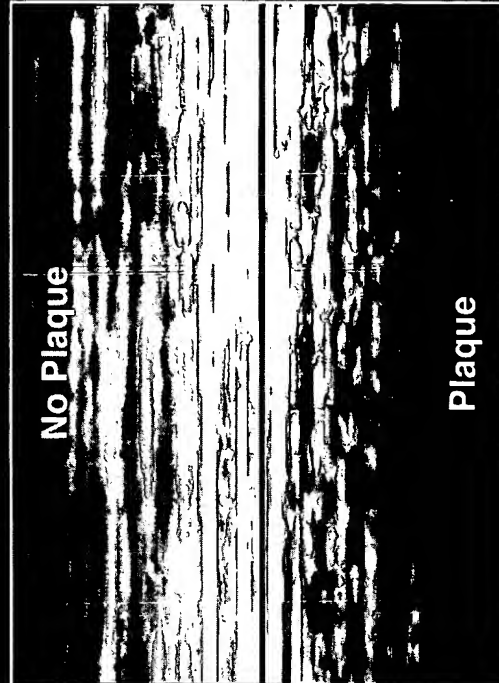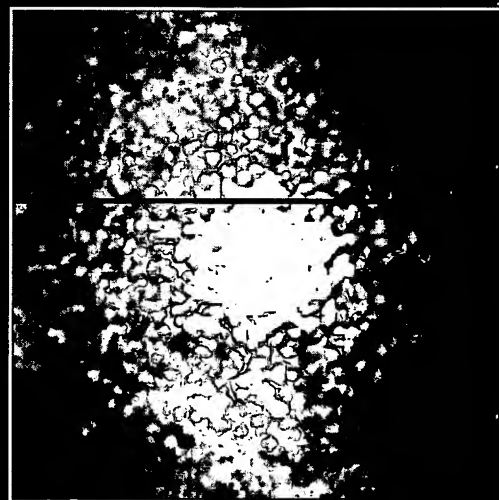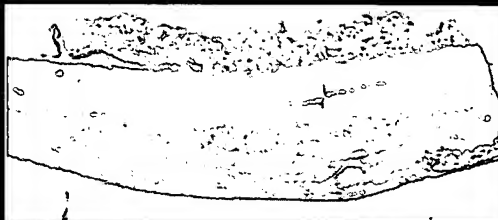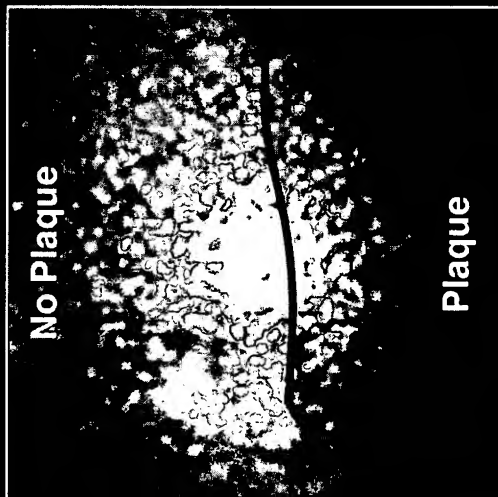
Feasibility Study Summary

Speckle decorrelation time constant is different between normal aorta and plaque

- $\tau = 500$ ms vs 40 ms

Speckle decorrelation time constant is different between thin and thick-walled plaques

- Greater for thick-walled plaques

Speckle decorrelation is spatially dependent

- Border between plaque and normal aorta demarcates different speckle decorrelation time constants

Clinical Realization

Catheter based technique (one possibility)

- Array of fibers
- Scanned probe

Transparent
Outer
Sheath

Fiber
Array

Inner Cable Motion

Difficulties

- Intrinsic heart and catheter motion
  - Lipid pool Brownian motion time constant is approximately 40 ms
- Blood
  - Will need saline infusion and/or direct contact with tissue

Alternative Methods
(Spatial Localization)

Localize time and space (x, y, z) dependent speckle patterns using optical methods as opposed to light diffusion

- Confocal microscopy
  - Apertures in the source and detector planes combined with a high numerical aperture imaging lens
  - High resolution speckle analysis in (x, y, z)
  - Speckle decorrelation is less sensitive than multiple scattering technique

- Optical Coherence Tomography (OCT)
  - Uses low coherence interferometry to obtain localization in z
  - Measures cap thickness directly
  - Speckle decorrelation is less sensitive than multiple scattering technique

Conclusion

Temporal and spatial analysis of the speckle patterns can potentially determine

- Cap thickness
- Cap and plaque viscosity
- Spatially resolved biomechanical stiffness
- <u>Plaque vulnerability</u>

Future work

- Speckle statistics
  - Can determine cap thickness and optical properties
  - Low coherence light
- Strain and stress measurements
  - Correlate biomechanical properties with Brownian motion measured by speckle decorrelation
- Probe development
- Continue cadaveric aorta studies
- In vivo studies (e.g. rabbit model)

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